PALM INTRANET

Day : Friday
Date: 9/10/2004
Time: 08:36:59

Inventor Name Search Result

Your Search was:

Last Name = SKEAD
First Name = BENJAMIN

Application#	Patent#	Status	Date Filed	Title	Inventor Name 9
60151769	Not Issued	159	08/31/1999	ENANTIOMERICALLY-ENRICHED COMPOUNDS HAVING PHOTOCLEAVABLE BOND(S) AND METHODS RELATED THERETO	SKEAD , BENJAMIN M.
60016991	Not Issued	159	05/07/1996	COMPOUNDS	SKEAD , BENJAMIN M.
60016987	Not Issued	159	05/07/1996	RESOLUTION	SKEAD , BENJAMIN M.
60016536	Not Issued	159	05/07/1996	RESOLUTION	SKEAD , BENJAMIN M.
10620396	Not Issued	030	07/16/2003	PROCESS FOR THE PREPARATION OF PHENYLALANINE ENAMIDE DERIVATIVES	SKEAD, BENJAMIN MARK
09652681	Not Issued	061	08/31/2000	ENANTIOMERICALLY-ENRICHED COMPOUNDS HAVING PHOTOCLEAVABLE BOND(S) AND METHODS RELATED THERETO	SKEAD, BENJAMIN M.
09650484	Not Issued	160	08/29/2000	ENANTIOMERICALLY-ENRICHED COMPOUNDS HAVING PHOTOCLEAVABLE BOND(S) AND METHODS RELATED THERETO	SKEAD, BENJAMIN M.
08849418	5994548	150	04/25/1997	CRYSTALLISATION OF LEVIBUPIVACAINE AND ANALOGUES THEREOF	SKEAD , BENJAMIN MARK
08796358	5892093	150	02/07/1997	RESOLUTION	SKEAD , BENJAMIN MARK

Inventor Search Completed: No Records to Display.

10/620,396 STN - Structure Search 9/10/04

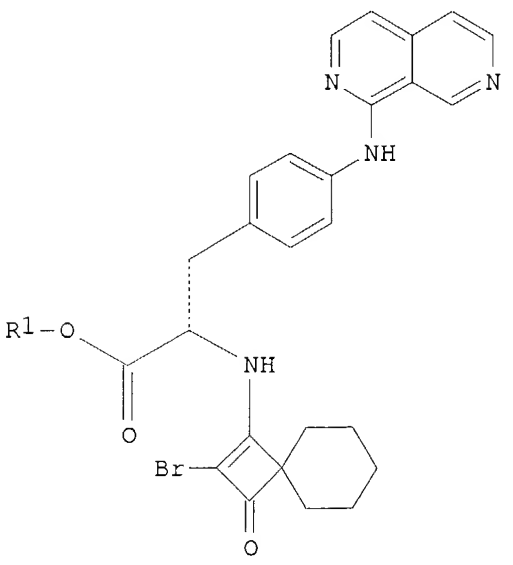
=> d ibib abs hitstr 1-13

L6 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60508 CAPLUS
DOCUMENT NUMBER: 140:94295
TITLE: Preparation of phenylalanine enamide derivatives containing a spiro[3.5]non-1-ene ring for use as integrin inhibitors
INVENTOR(S): Brown, Julien Alistair; Bailey, Stuart; Brand, Stephen
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007494	A1	20040122	WO 2003-GB3104	20030716

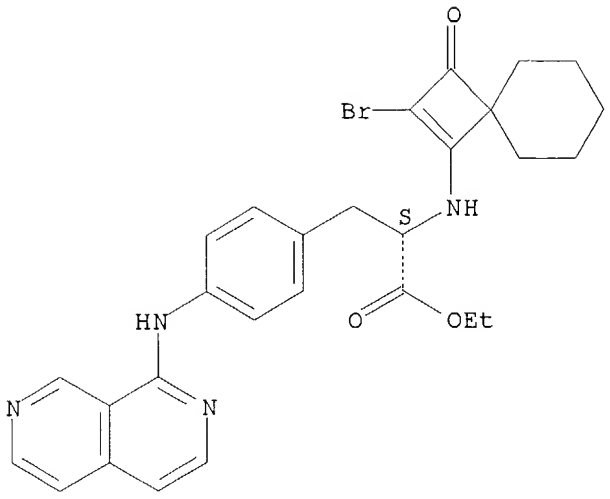
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-16571 A 20020717
GI



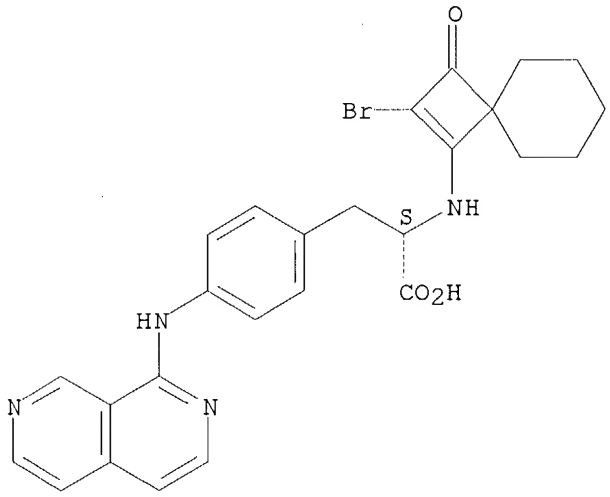
I

AB Phenylalanine enamide derivs. I [R1 = iso-Pr, Pr, Me3CCH2, CH2CH2OH or -OMe, CH2CH2OCH2CH2OH or -OMe, 2-morpholinoethyl, 2-(4-methyl-1-



RN 455264-31-0 CAPLUS
CN L-Phenylalanine, N-(2-bromo-3-oxospiro[3.5]non-1-en-1-yl)-4-(2,7-naphthyridin-1-ylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



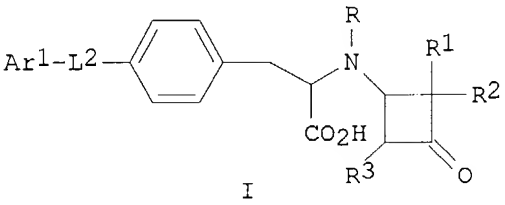
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60451 CAPLUS
DOCUMENT NUMBER: 140:94294
TITLE: Process for the preparation of phenylalanine enamide derivatives
INVENTOR(S): Skead, Benjamin Mark; Tyrrell, Nicholas David; Jones, Stephen Wilfred; Brookes, Michael Handforth
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007428	A1	20040122	WO 2003-GB3108	20030716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004073033	A1	20040415	US 2003-620396	20030716
PRIORITY APPLN. INFO.:			GB 2002-16574 A	20020717
OTHER SOURCE(S):	MARPAT 140:94294			

GI



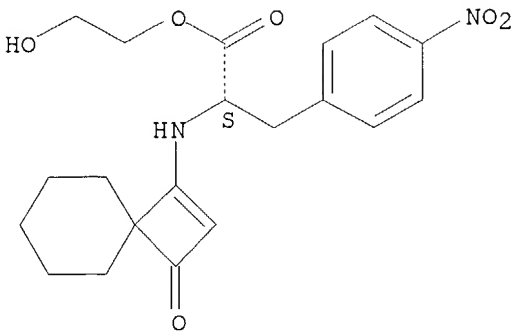
I

AB The invention describes a process for the preparation of phenylalanine enamide derivs. I [Ar1 is an (un)substituted aromatic or heteroarom. group; L2 is a linker group NH, CONH, SO2NH or N-alkyl derivs.; R is H or alkyl; R1, R2, R3 are -L1-Alk10-1-R41-3, where L1 is a covalent bond or a linker atom or group, Alk1 is an (un)substituted aliphatic or heteroaliph. chain, R4 is H, halo, OH, (cyclo)alkoxy, (cyclo)alkylthio, CN, or an (un)substituted (hetero)cycloaliph., (hetero)polycycloaliph., or (hetero)aromatic group; or R1 and R2 are joined together to form an (un)substituted spiro-linked (hetero)cycloaliph. group], including their salts, solvates, hydrates and N-oxides, which comprises reacting a p-amino- or p-(alkylamino)phenylalanine derivative with a compound Ar1-W, where W is a leaving group, CO2H, a carbonyl or sulfonyl halide. Thus, Et 2(S)-[(3-oxospiro[3.5]non-1-enyl)amino]-3-[4-[(3,5-dichloroisonicotinoyl)amino]phenyl]propionate was prepared by acylation of Et 3-(4-aminophenyl)-2(S)-[(3-oxospiro[3.5]non-1-enyl)amino]propionate (II) with 3,5-dichloroisonicotinoyl chloride. Intermediate II was prepared by reaction of 4-nitro-L-phenylalanine Et ester with spiro[3.5]nonane-1,3-dione.

IT **455262-36-9P 455262-41-6P 455262-42-7P 455264-29-6P 644995-17-5P 644995-18-6P 644995-20-0P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(process for preparation of phenylalanine enamide derivs.)

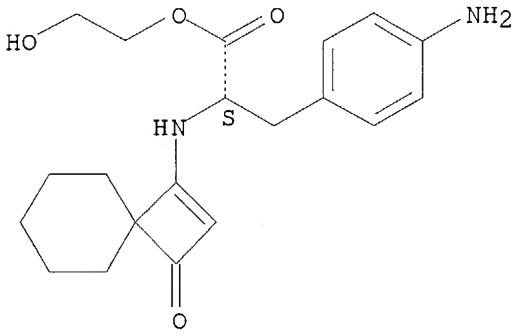
RN 455262-36-9 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(3-oxospiro[3.5]non-1-en-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 644995-16-4 CAPLUS
CN L-Phenylalanine, 4-amino-N-(3-oxospiro[3.5]non-1-en-1-yl)-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60307 CAPLUS
DOCUMENT NUMBER: 140:94293
TITLE: Preparation of phenylalanine enamide derivatives containing a spiro[3.5]non-1-ene ring for use as integrin inhibitors
INVENTOR(S): Brown, Julien Alistair; Bailey, Stuart; Brand, Stephen
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

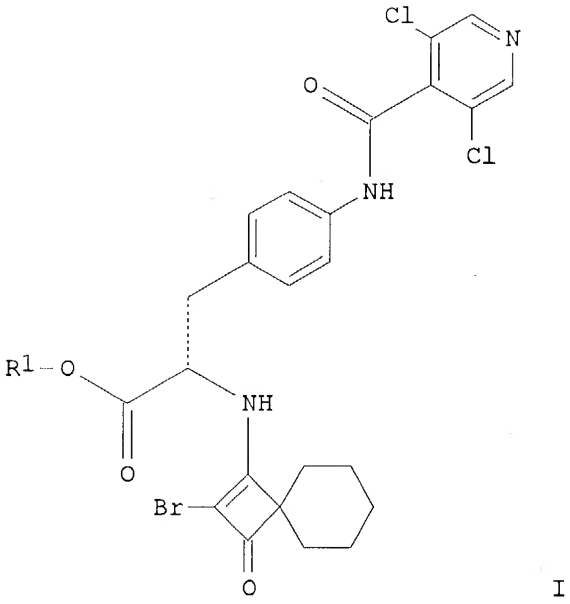
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006918	A1	20040122	WO 2003-GB3100	20030716

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,

TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-16568 A 20020717

GI



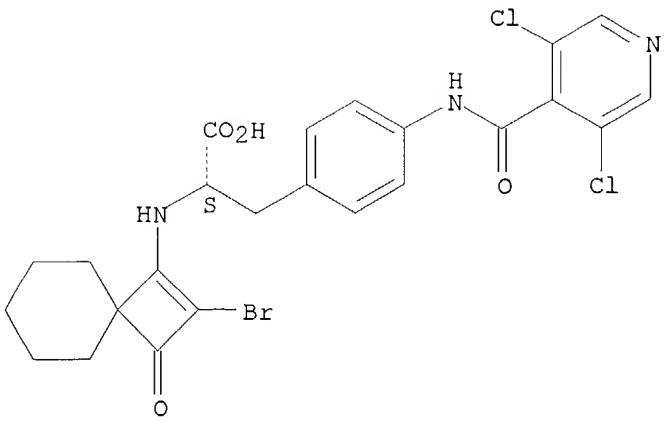
I

AB Phenylalanine enamide derivs. I [R1 = Me, Bu, CH2CH2OH or -OMe, CH2CH2OCH2CH2OH or -OMe, 2-morpholinoethyl, 2-(4-methyl-1-piperazinyl)ethyl] or their salts, solvates and N-oxides were prepared as potent and selective inhibitors of α4 integrins. The compds. are of use in modulating cell adhesion and in particular are of use in the prophylaxis and treatment of diseases or disorders including inflammation in which the extravasation of leukocytes plays a role. Thus, I (R1 = CH2CH2OH) was prepared by condensation of Et (2S)-2-amino-3-[4-[(3,5-dichloroisonicotinoyl)amino]phenyl]propanoate (preparation given) with 1-oxo-3-hydroxyspiro[3.5]none-2-ene, followed by bromination, saponification, and esterification with ethylene glycol. The product has an IC50 value of 4 nM in the α4β1 assay.

IT **644967-49-7P 644967-50-0P 644967-51-1P 644967-52-2P 644967-53-3P 644967-54-4P 644967-55-5P 644967-56-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of phenylalanine spirononenone derivs. for use as integrin inhibitors)

RN 644967-49-7 CAPLUS

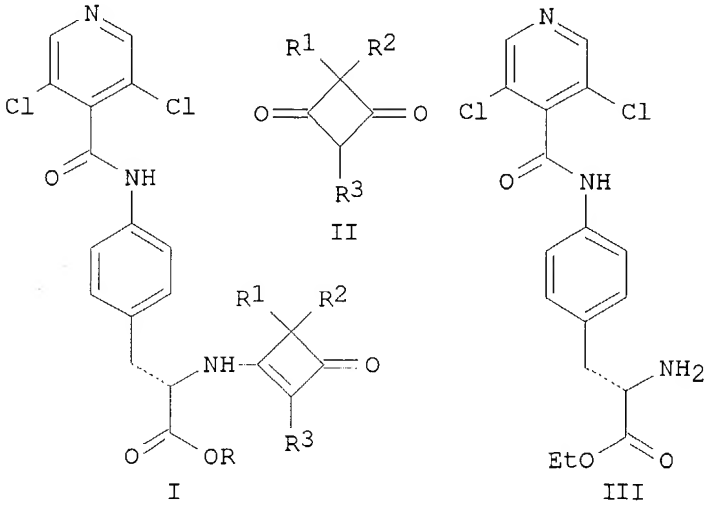
CN L-Phenylalanine, N-(2-bromo-3-oxospiro[3.5]non-1-en-1-yl)-4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

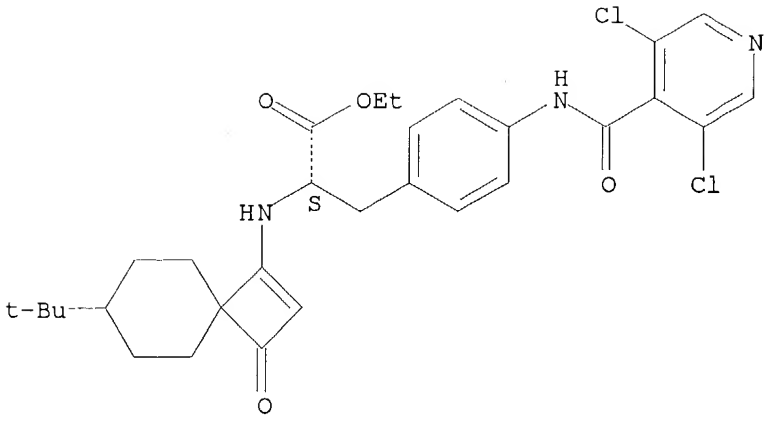


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:435940 CAPLUS
DOCUMENT NUMBER: 139:149503
TITLE: Efficient Synthesis of 3-Aminocyclobut-2-en-1-ones: Squaramide Surrogates as Potent VLA-4 Antagonists
AUTHOR(S): Brand, Stephen; De Candole, Benjamin C.; Brown, Julien A.
CORPORATE SOURCE: Medicinal Chemistry, Celltech Group plc, Slough, SL1 4EN, UK
SOURCE: Organic Letters (2003), 5(13), 2343-2346
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:149503
GI

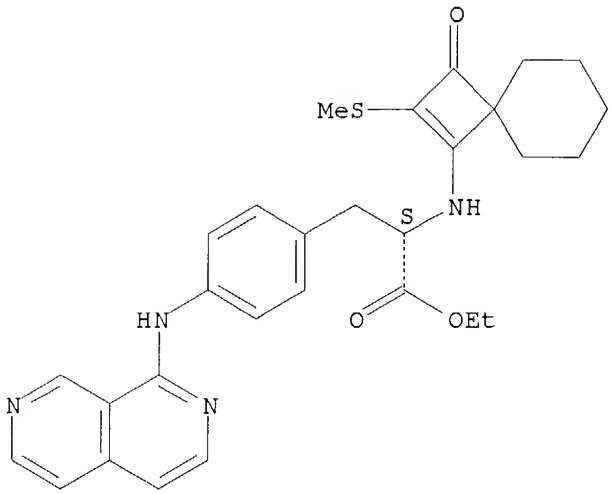




REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:675997 CAPLUS
DOCUMENT NUMBER: 137:217241
TITLE: Preparation of phenylalanine enamide derivatives possessing a cyclobutene group for use as integrin inhibitors
INVENTOR(S): Bailey, Stuart; Brown, Julien Alistair; Brand, Stephen; Johnson, James Andrew; Porter, John Robert; Head, John Clifford
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068393	A1	20020906	WO 2002-GB206	20020118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2387845	A1	20031029	GB 2003-18429	20020118
EP 1370531	A1	20031217	EP 2002-715515	20020118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007166	A	20040210	BR 2002-7166	20020118
JP 2004524313	T2	20040812	JP 2002-567907	20020118
US 2002169336	A1	20021114	US 2002-81072	20020222
NO 2003003710	A	20031022	NO 2003-3710	20030820
PRIORITY APPLN. INFO.:			GB 2001-4418 A	20010222
			GB 2001-14000 A	20010608
			GB 2001-27562 A	20011116



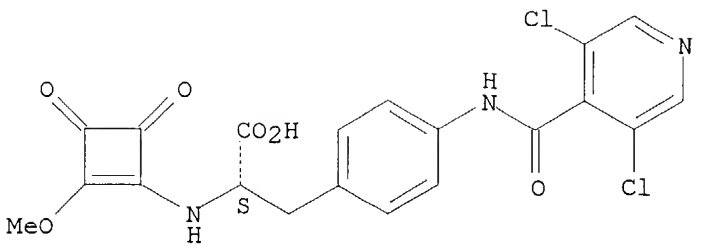
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:211229 CAPLUS
DOCUMENT NUMBER: 137:210402
TITLE: Squaric acid derivatives as VLA-4 integrin antagonists
AUTHOR(S): Porter, John R.; Archibald, Sarah C.; Childs, Kirstie; Critchley, David; Head, John C.; Linsley, Janeen M.; Parton, Ted A. H.; Robinson, Martyn K.; Shock, Anthony; Taylor, Richard J.; Warrellow, Graham J.; Alexander, Rikki P.; Langham, Barry
CORPORATE SOURCE: Celltech R&D Ltd., Slough, SL1 4EN, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(7), 1051-1054
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:210402

AB SAR studies aimed at improving the rate of clearance by the incorporation of a 3,4-diamino-3-cyclobutene-1,2-dione group as an amino acid isostere in a series of VLA-4 integrin antagonists are described.

IT **312292-16-3P 312293-18-8P 312293-32-6P**
312293-42-8P 312293-43-9P 312293-44-0P
312293-49-5P 312293-50-8P 312293-56-4P
312293-57-5P 312293-58-6P 312293-59-7P
312293-61-1P 312293-65-5P 312293-68-8P
312293-69-9P 312293-70-2P 312293-71-3P
312293-73-5P 312293-74-6P 312293-81-5P
312293-82-6P 312293-89-3P 312293-90-6P
312293-91-7P 312293-92-8P 312294-01-2P
312294-02-3P 455894-84-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(squaric acid derivs. as VLA-4 integrin antagonists)

RN 312292-16-3 CAPLUS
CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:107317 CAPLUS
DOCUMENT NUMBER: 136:167287
TITLE: Preparation of novel 3-substituted isoquinolin-1-yl derivatives of squaric acid amides as selective α4-integrin inhibitors
INVENTOR(S): Head, John Clifford; Porter, John Robert; McKay, Catherine
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010136	A1	20020207	WO 2001-GB3429	20010730
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1305291	A1	20030502	EP 2001-953234	20010730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004505110	T2	20040219	JP 2002-516268	20010730
US 6469025	B1	20021022	US 2001-920206	20010801
US 2002177605	A1	20021128		

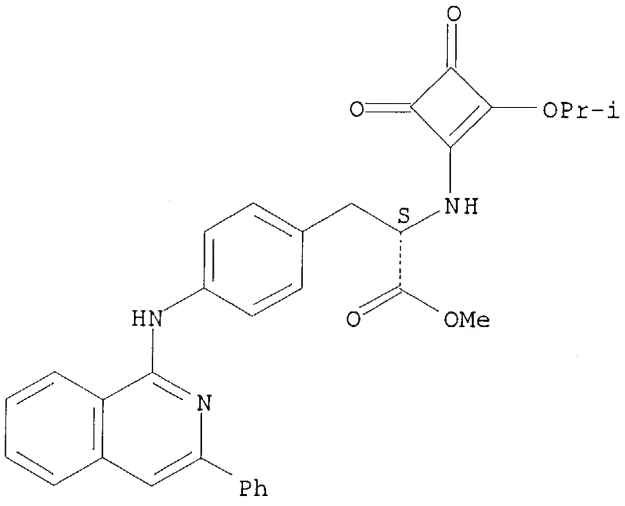
PRIORITY APPLN. INFO.:

GB 2000-18969	A	20000802
GB 2000-28837	A	20001127
WO 2001-GB3429	W	20010730

OTHER SOURCE(S): MARPAT 136:167287
GI

isoquinolinylamino)phenyl]-2-(2-isopropoxy-3,4-dioxocyclobut-1-enylamino)propanoate
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of 3-substituted isoquinolin-1-yl derivs. of squaric acid amides as α4-integrin inhibitors)
RN 395093-29-5 CAPLUS
CN L-Phenylalanine, N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-phenyl-1-isoquinolinyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:51439 CAPLUS
DOCUMENT NUMBER: 136:118460
TITLE: Preparation of squaric acid derivatives containing a bicyclic heteroaromatic ring as integrin antagonists
INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrellow, Graham John
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004426	A1	20020117	WO 2001-GB3028	20010705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

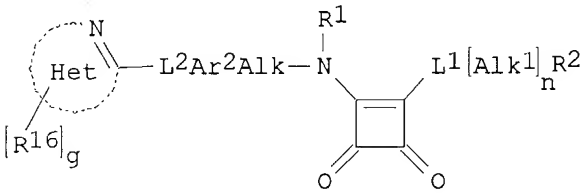
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002107263	A1	20020808	US 2001-899488	20010705
US 6740654	B2	20040525		
EP 1301488	A1	20030416	EP 2001-945540	20010705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502762	T2	20040129	JP 2002-509293	20010705

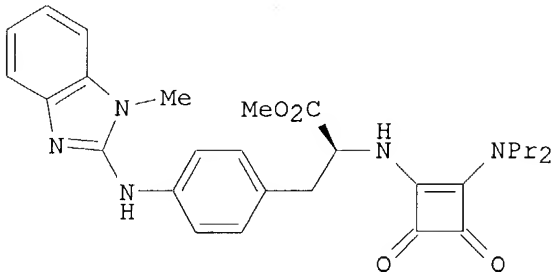
PRIORITY APPLN. INFO.:
GB 2000-16785 A 20000707
GB 2000-28364 A 20001121
WO 2001-GB3028 W 20010705

OTHER SOURCE(S): MARPAT 136:118460

GI



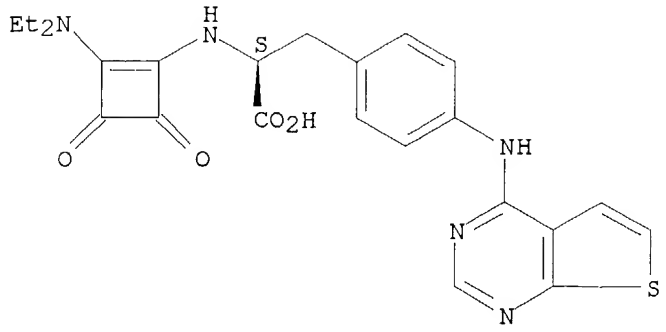
I



II

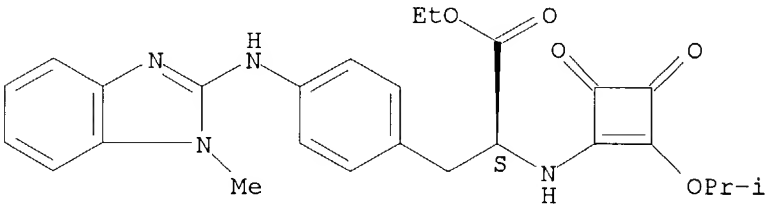
AB The title compds. [I; Het = (un)substituted bicyclic fused ring heteroarom. group; R16 = H, alkyl, etc.; g = 0-4; L2 = a bond, O, S, CO, etc.; Ar2 = (un)substituted (hetero)aromatic; Alk = CH2CHR, CH:CR, CH(CH2R), C(:CHR) (wherein R = CO2H or a derivative or biostere thereof); R1 = H, alkyl; L1 = a covalent bond, a linker atom or group; Alk1 = (un)substituted aliphatic chain; n = 0-1; R2 = H, (un)substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloalphatic, heteropolycycloaliph., aromatic or heteroarom. group other than a 2,6-naphthyridin-1-yl, isoquinolin-1-yl, 2,7-naphthyridin-1-yl or quinazolin-4-yl] which are able to inhibit the binding of integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders, or disorders involving the inappropriate growth or migration of cells, were prepared Thus, reacting Et (S)-2-amino-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoate.CF3CO2H with diisopropylsquarate in the presence of DIPEA in iso-Pr followed by treatment of the resulting Et (S)-2-{[2-(isopropoxy)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoate with dipropylamine in MeOH afforded II. The exemplified compds. I showed IC50 of ≤ 1 μM in the α4β1 and α4β7 assays.

IT **389637-00-7P 389637-01-8P 389637-02-9P 389637-06-3P 389637-07-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of squaric acid derivs. containing a bicyclic heteroarom. ring as



IT **389637-11-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of squaric acid derivs. containing a bicyclic heteroarom. ring as
integrin antagonists)
RN 389637-11-0 CAPLUS
CN L-Phenylalanine, 4-[(1-methyl-1H-benzimidazol-2-yl)amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:886114 CAPLUS
DOCUMENT NUMBER: 136:20059
TITLE: Preparation of naphthyridine squaric acid derivatives as integrin inhibitors.
INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrellow, Graham John
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092256	A1	20011206	WO 2001-GB2425	20010530

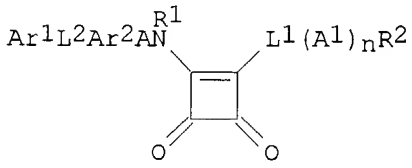
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002115684	A1	20020822	US 2001-867016		20010529
US 6545013	B2	20030408			
EP 1286995	A1	20030305	EP 2001-934177		20010530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003535088	T2	20031125	JP 2002-500869		20010530
PRIORITY APPLN. INFO.:			GB 2000-13101	A	20000530
			GB 2000-28841	A	20001127
			WO 2001-GB2425	W	20010530

OTHER SOURCE(S): MARPAT 136:20059

GI



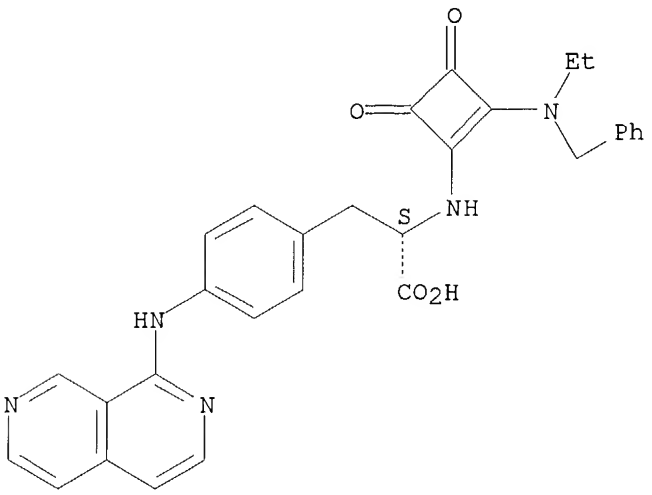
I

AB Title compds. [I; Ar1 = (substituted) 2,7-naphthridin-1-yl; L2 = bond, linker atom or group; Ar2 = (substituted) aromatic or heteroarom. chain; A = CH2CHR, CH:CR, CHCH2R, C:CHR; R = CO2H or a derivative or biostere thereof; R1 = H, alkyl; L1 = bond, linker atom or group; A1 = (substituted) aliphatic chain; n = 0, 1; R2 = H, (substituted) heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., heteropolycycloaliph., aryl, heteroaryl] and the salts, solvates, hydrates and N-oxides thereof, were prepared Thus, a mixture of 1,2-diisopropoxy-3,4-dioxocyclobut-1-ene and Et (S)-3-[4-(2,7-naphthyridin-1-ylamino)phenyl]-2-aminopropanoate (preparation given) in EtOH was stirred at 50° overnight to give 79% Et (S)-3-[4-(2,7-naphthyridin-1-ylamino)phenyl]-2-(2-isopropoxy-3,4-dioxocyclobut-1-enylamino)propanoate. Tested I in α4β1 and α4β7 screens inhibited cell adhesion with IC50 ≤1 μM.

IT **378251-41-3P 378251-42-4P 378251-43-5P**
378251-44-6P 378251-45-7P 378251-47-9P
378251-48-0P 378251-49-1P 378251-50-4P
378251-51-5P 378251-53-7P 378251-55-9P
378251-57-1P 378251-58-2P 378251-59-3P
378251-61-7P 378251-62-8P 378251-63-9P
378251-73-1P 378251-74-2P 378251-75-3P
378251-76-4P 378251-77-5P 378251-78-6P
378251-79-7P 378251-80-0P 378251-81-1P
378251-82-2P 378251-85-5P 378251-86-6P
378252-20-1P 378252-21-2P 378252-22-3P
378252-23-4P 378252-27-8P 378252-28-9P
378252-29-0P 378252-35-8P 378252-41-6P
378252-42-7P 378252-43-8P 378252-44-9P
378252-45-0P 378252-46-1P 378252-47-2P
378252-48-3P 378252-49-4P 378252-50-7P

RN 378252-73-4 CAPLUS
CN L-Phenylalanine, N-[2-[ethyl(phenylmethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-(2,7-naphthyridin-1-ylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

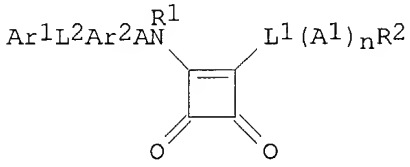


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:886077 CAPLUS
DOCUMENT NUMBER: 136:20029
TITLE: Preparation of squaric acid isoquinoline derivatives as integrin binding inhibitors.
INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrelow, Graham John
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092233	A1	20011206	WO 2001-GB2390	20010530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6403608	B1	20020611	US 2001-867060	20010529
EP 1284967	A1	20030226	EP 2001-934158	20010530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

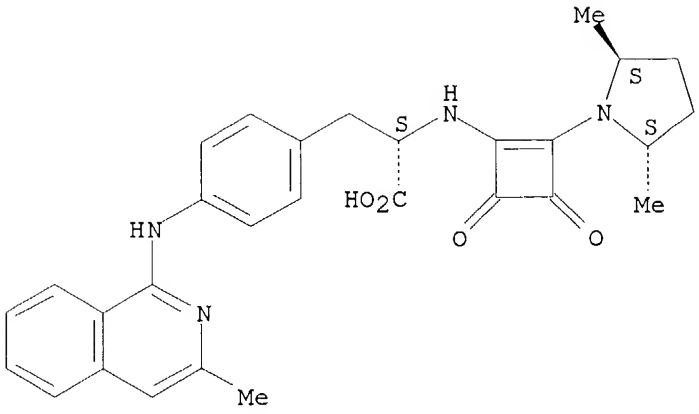
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003535081 T2 20031125 JP 2002-500847 20010530
PRIORITY APPLN. INFO.: GB 2000-13087 A 20000530
GB 2000-19060 A 20000803
GB 2000-28842 A 20001127
WO 2001-GB2390 W 20010530
OTHER SOURCE(S): MARPAT 136:20029
GI



I

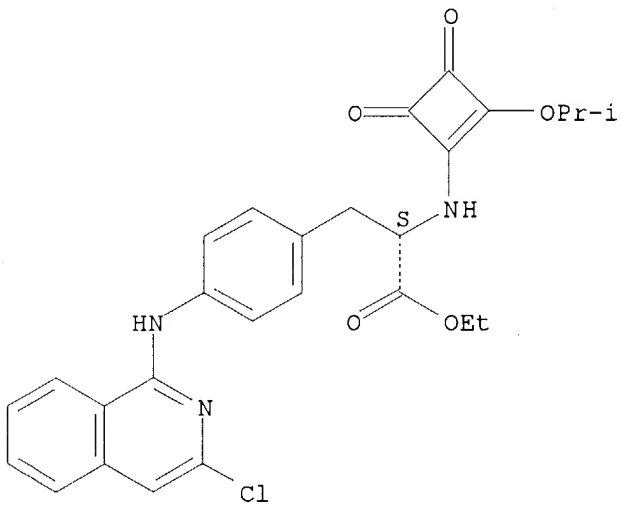
AB Title compds. [I; Ar1 = 3-substituted isoquinolin-1-yl; L1, L2 = bond, linker atom or group; Ar2 = (substituted) aromatic or heteroanomatic chain; A = CH2CHR, CH:CR, CH(CH2R), C(:CHR); R = CO2H or a derivative or biostere thereof; R1 = H, alkyl; A1 = (substituted) aliphatic chain; n = 0, 1; R2 = H, (substituted) heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., heteropolycycloalkyl], were prepared as integrin binding inhibitors (no data). Thus, Me (S)-2-amino-3-[4-(3-ethyl-1-isoquinolinylamino)phenyl]propanoate (preparation given), 3,4-diisopropoxy-3-cyclobuten-1,2-dione, and diisopropylethylamine were stirred 16 h in MeOH to give 100% Me (S)-3-[4-(3-ethyl-1-isoquinolinylamino)phenyl]-2-[(2-isopropoxy-3,4-dioxocyclobut-1-enyl)amino]propanoate. I generally show IC50 ≤1 μM in integrin α4β1 and α4β7 cell adhesion inhibition assays.

IT **378234-59-4P 378234-60-7P 378234-61-8P**
378234-62-9P 378234-63-0P 378234-64-1P
378234-65-2P 378234-66-3P 378234-67-4P
378234-68-5P 378234-69-6P 378234-71-0P
378234-72-1P 378234-73-2P 378234-74-3P
378234-75-4P 378234-76-5P 378234-77-6P
378234-78-7P 378234-79-8P 378234-80-1P
378234-82-3P 378234-83-4P 378234-84-5P
378234-85-6P 378234-86-7P 378234-87-8P
378234-88-9P 378234-89-0P 378234-90-3P
378234-91-4P 378234-93-6P 378234-94-7P
378234-95-8P 378234-96-9P 378234-97-0P
378234-98-1P 378234-99-2P 378235-00-8P
378235-01-9P 378235-03-1P 378235-04-2P
378235-05-3P 378235-06-4P 378235-07-5P
378235-08-6P 378235-10-0P 378235-11-1P
378235-12-2P 378235-13-3P 378235-14-4P
378235-15-5P 378235-16-6P 378235-17-7P
378235-18-8P 378235-19-9P 378235-31-5P
378235-32-6P 378235-75-7P 378235-76-8P
378235-77-9P 378235-78-0P 378235-79-1P
378235-80-4P 378235-81-5P 378235-82-6P
378235-83-7P 378235-84-8P 378235-85-9P
378235-86-0P 378235-87-1P 378235-88-2P
378235-89-3P 378235-90-6P 378235-91-7P
378235-92-8P 378235-93-9P 378235-94-0P
378235-95-1P 378235-96-2P 378235-97-3P
378235-98-4P 378235-99-5P 378236-00-1P
378236-01-2P 378236-02-3P 378236-03-4P



IT **378236-44-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of squaric acid isoquinoline derivs. as integrin binding inhibitors)
RN 378236-44-3 CAPLUS
CN L-Phenylalanine, 4-[(3-chloro-1-isoquinolinyl)amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



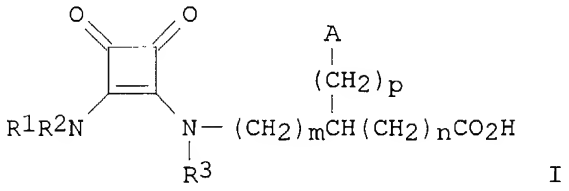
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:909217 CAPLUS
DOCUMENT NUMBER: 134:56962
TITLE: Preparation of 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Lombardo, Louis J.; Sabalski, Joan
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6166050	A	20001226	US 1999-458852	19991210
PRIORITY APPLN. INFO.:			US 1998-155221P P	19981214
OTHER SOURCE(S):	MARPAT 134:56962			

GI



I

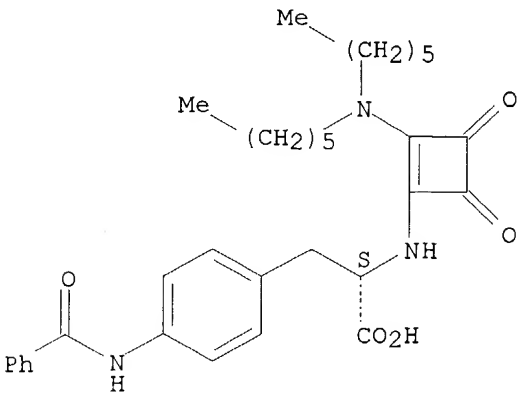
AB Diaminocyclobutenedione amino acid derivs. I (R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or R1R2N form a saturated or unsatd. heterocyclic ring; R3 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; A = aryl, heteroaryl; m, n, p = 0-3) were prepared for the treatment of inflammatory and autoimmune diseases. Thus, N-[2-(benzylamino)-3,4-dioxocyclobut-1-enyl]-L-phenylalanine, prepared by treatment of L-phenylalanine Me ester hydrochloride with 3,4-diethoxy-3-cyclobutene-1,2-dione and benzylamine and saponification, showed IC50 = 58 μM for binding of α4β1 integrin (VLA-4).

IT **274927-11-6P 274927-20-7P 274927-22-9P**
274927-24-1P 274927-26-3P 274927-29-6P
274927-31-0P 274927-33-2P 274927-38-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

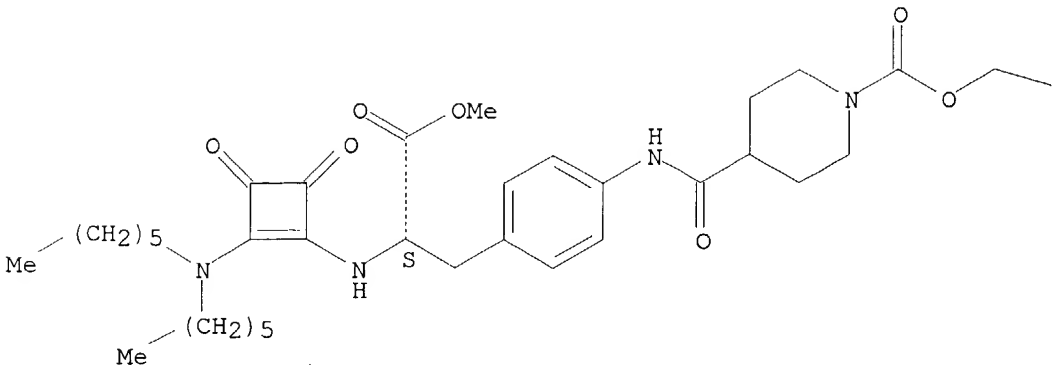
RN 274927-11-6 CAPLUS

CN L-Phenylalanine, 4-(benzoylamino)-N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A



PAGE 1-B

Ph

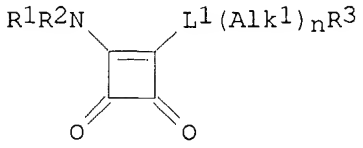
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:861644 CAPLUS
DOCUMENT NUMBER: 134:29705
TITLE: Preparation of squaric acid derivatives as cell adhesion molecules
INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrelow, Graham John
PATENT ASSIGNEE(S): Celltech Chiroscience Limited, UK
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073260	A1	20001207	WO 2000-GB2020	20000526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6518283	B1	20030211	US 2000-579317	20000525
EP 1181266	A1	20020227	EP 2000-935341	20000526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2003500467	T2	20030107	JP 2000-621327		20000526
US 2003162799	A1	20030828	US 2002-319272		20021213
PRIORITY APPLN. INFO.:			GB 1999-12640	A	19990528
			GB 2000-2858	A	20000208
			US 2000-579317	A3	20000525
			WO 2000-GB2020	W	20000526

OTHER SOURCE(S): MARPAT 134:29705
GI



I

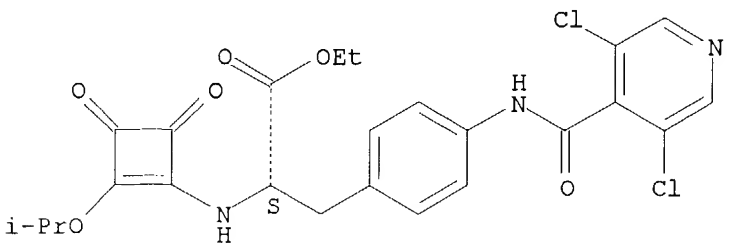
AB Squaric acid derivs. I [R1 is an integrin binding group; R2 is a hydrogen atom or a C1-6 alkyl group; L1 is a covalent bond or a linker atom or group; n = 0, 1; Alk1 is an optionally substituted aliphatic chain; R3 is H or an optionally substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., polyheterocycloaliph., aromatic or heteroarom. group] and their salts, solvates, hydrates and N-oxides were prepared as inhibitors of the binding of integrins to their ligands. Thus, treatment of Et (S)-3-(4-aminophenyl)-2-(tert-butoxycarbonylamino)propionate with 3,5-dichloro-4-pyridinecarboxylic acid, deprotection, reaction with 3,4-diisopropoxy-3-cyclobutene-1,2-dione, propylamination, and saponification afforded (S)-3-[4-(3,5-dichloro-4-pyridylcarboxamido)phenyl]-2-(2-propylamino-3,4-dioxocyclobut-1-enylamino)propanoic acid. Compds. of the invention in which R1 is an α4 integrin binding group generally have IC50 values <1 μM in the α4β1 and α4β7 assays.

IT **312292-12-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(Preparation of squaric acid derivs. as cell adhesion mols.)

RN 312292-12-9 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **312292-13-0P 312292-15-2P 312292-17-4P**
312292-21-0P 312292-23-2P 312292-24-3P
312292-25-4P 312292-67-4P 312292-68-5P
312292-86-7P 312293-01-9P 312293-02-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

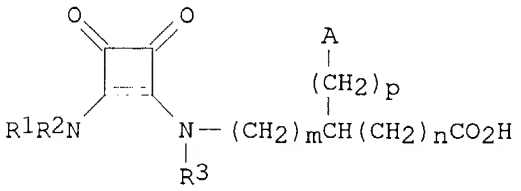
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:421084 CAPLUS
DOCUMENT NUMBER: 133:43808
TITLE: Preparation of 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Lombardo, Louis John; Sabalski, Joan E.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035855	A1	20000622	WO 1999-US29369	19991210
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9916211	A	20010911	BR 1999-16211	19991210
EP 1140792	A1	20011010	EP 1999-967265	19991210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-211183 A 19981214
WO 1999-US29369 W 19991210

OTHER SOURCE(S): MARPAT 133:43808
GI



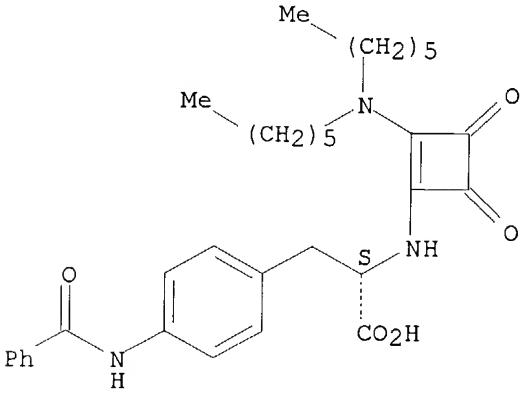
I

AB Diaminocyclobutenedione amino acid derivs. I (R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or R1R2N form a saturated or unsatd. heterocyclic ring; R3 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; A = aryl, heteroaryl; m, n, p = 0-3) were prepared for the treatment of inflammatory and autoimmune diseases. Thus, N-[2-(benzylamino)-3,4-dioxocyclobut-1-enyl]-L-phenylalanine, prepared by treatment of L-phenylalanine Me ester hydrochloride with 3,4-diethoxy-3-cyclobutene-1,2-dione and benzylamine and saponification, showed IC50 for binding of the α4β1 integrin (VLA-4).

IT **274927-11-6P 274927-20-7P 274927-22-9P**
274927-24-1P 274927-26-3P 274927-29-6P
274927-31-0P 274927-33-2P 274927-38-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

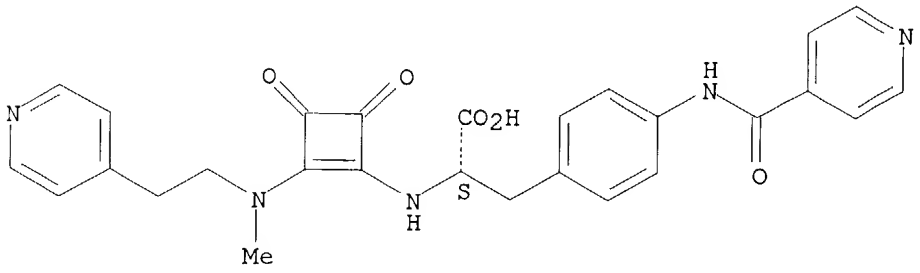
RN 274927-11-6 CAPLUS
CN L-Phenylalanine, 4-(benzoylamino)-N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



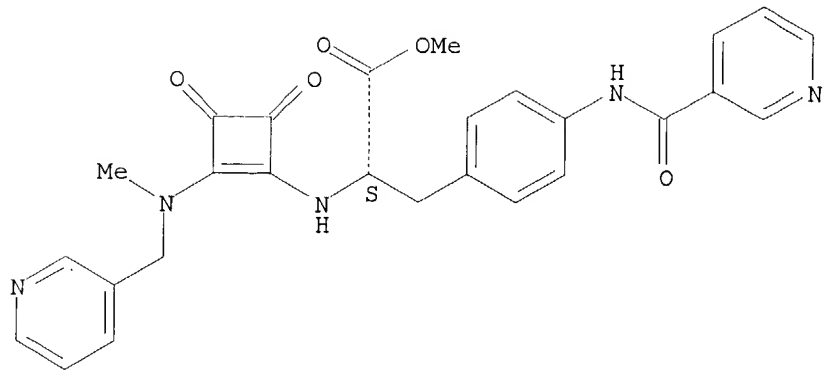
RN 274927-20-7 CAPLUS
CN L-Phenylalanine, N-[2-[methyl[2-(4-pyridinyl)ethyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



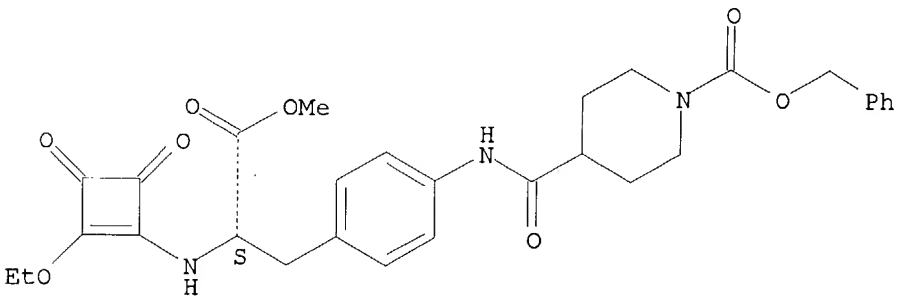
RN 274927-22-9 CAPLUS
CN L-Phenylalanine, N-[2-[methyl(2-phenylethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



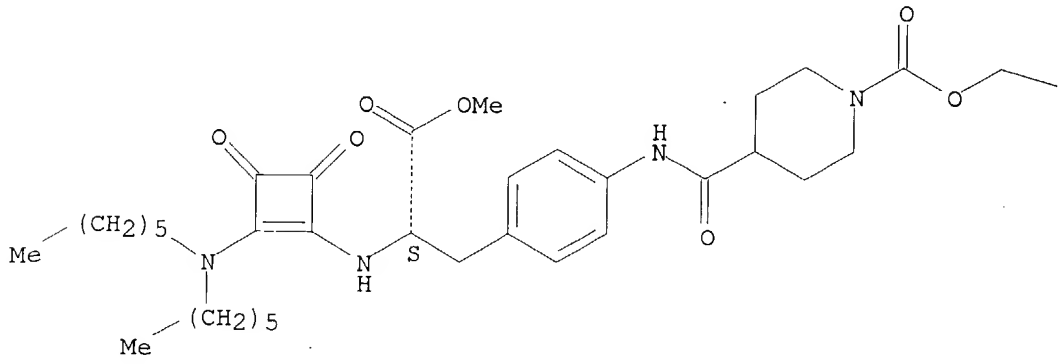
RN 274927-36-5 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[[4-[(2S)-2-[(2-ethoxy-3,4-dioxo-1-cyclobuten-1-yl)amino]-3-methoxy-3-oxopropyl]phenyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274927-37-6 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[[4-[(2S)-2-[[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]amino]-3-methoxy-3-oxopropyl]phenyl]amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Ph

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

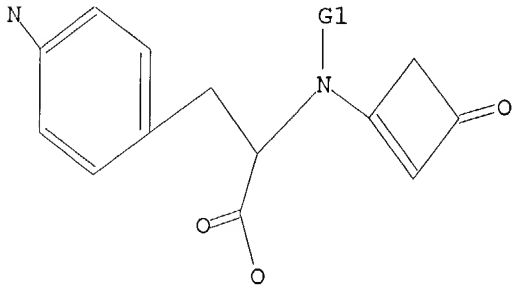
=> d his

(FILE 'HOME' ENTERED AT 09:09:54 ON 10 SEP 2004)

FILE 'REGISTRY' ENTERED AT 09:10:12 ON 10 SEP 2004
L1 STRUCTURE UPLOADED
L2 34 S L1
L3 690 S L1 FULL

FILE 'CAPLUS' ENTERED AT 09:12:31 ON 10 SEP 2004
L4 13 S L3/PREP
L5 13 S L3
L6 13 S L4 OR L5

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

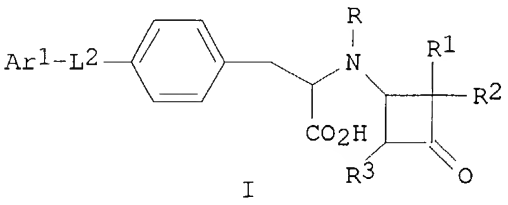
=>

=> d ibib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60451 CAPLUS
DOCUMENT NUMBER: 140:94294
TITLE: Process for the preparation of phenylalanine enamide derivatives
INVENTOR(S): Skead, Benjamin Mark; Tyrrell, Nicholas David; Jones, Stephen Wilfred; Brookes, Michael Handforth
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007428	A1	20040122	WO 2003-GB3108	20030716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004073033	A1	20040415	US 2003-620396	20030716
PRIORITY APPLN. INFO.:			GB 2002-16574 A	20020717

OTHER SOURCE(S): MARPAT 140:94294
GI



I

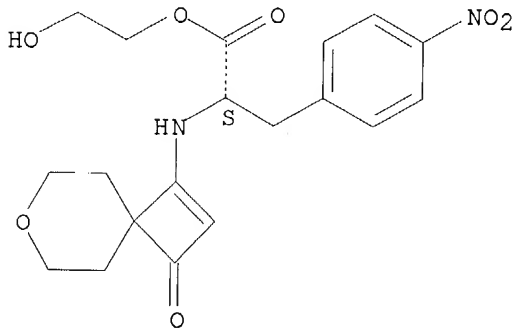
AB The invention describes a process for the preparation of phenylalanine enamide derivs. I [Ar1 is an (un)substituted aromatic or heteroarom. group; L2 is a linker group NH, CONH, SO2NH or N-alkyl derivs.; R is H or alkyl; R1, R2, R3 are -L1-Alk1-0-1-R41-3, where L1 is a covalent bond or a linker atom or group, Alk1 is an (un)substituted aliphatic or heteroaliph. chain, R4 is H, halo, OH, (cyclo)alkoxy, (cyclo)alkylthio, CN, or an (un)substituted (hetero)cycloaliph., (hetero)polycycloaliph., or (hetero)aromatic group; or R1 and R2 are joined together to form an (un)substituted spiro-linked (hetero)cycloaliph. group], including their salts, solvates, hydrates and N-oxides, which comprises reacting a p-amino- or p-(alkylamino)phenylalanine derivative with a compound Ar1-W, where W is a leaving group, CO2H, a carbonyl or sulfonyl halide. Thus, Et 2(S)-[(3-oxospiro[3.5]non-1-enyl)amino]-3-[4-[(3,5-dichloroisonicotinoyl)amino]phen

yl]propionate was prepared by acylation of Et 3-(4-aminophenyl)-2(S)-[(3-oxospiro[3.5]non-1-enyl)amino]propionate (II) with 3,5-dichloroisonicotinoyl chloride. Intermediate II was prepared by reaction of 4-nitro-L-phenylalanine Et ester with spiro[3.5]nonane-1,3-dione.

IT **644995-21-1P 644995-22-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparation of phenylalanine enamide derivs.)

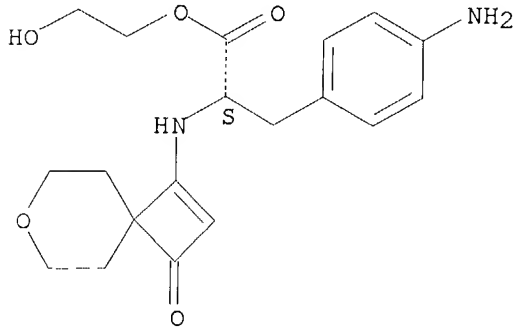
RN 644995-21-1 CAPLUS
CN L-Phenylalanine, 4-nitro-N-(3-oxo-7-oxaspiro[3.5]non-1-en-1-yl)-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 644995-22-2 CAPLUS
CN L-Phenylalanine, 4-amino-N-(3-oxo-7-oxaspiro[3.5]non-1-en-1-yl)-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

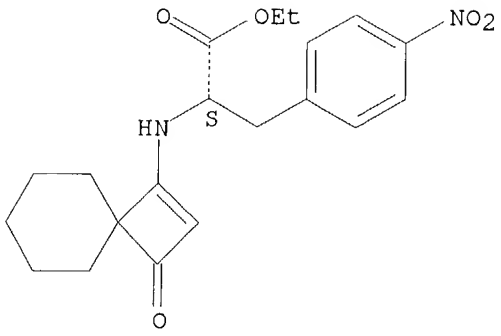
Absolute stereochemistry.



IT **644995-08-4P 644995-09-5P 644995-10-8P**
644995-11-9P 644995-12-0P 644995-13-1P
644995-15-3P 644995-16-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of phenylalanine enamide derivs.)

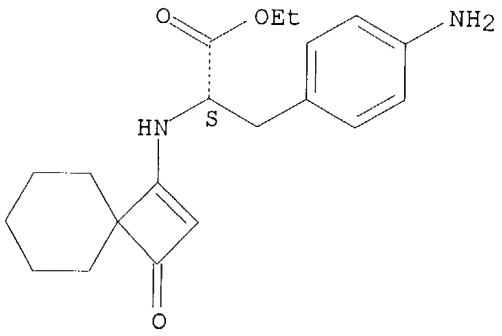
RN 644995-08-4 CAPLUS
CN L-Phenylalanine, 4-nitro-N-(3-oxospiro[3.5]non-1-en-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



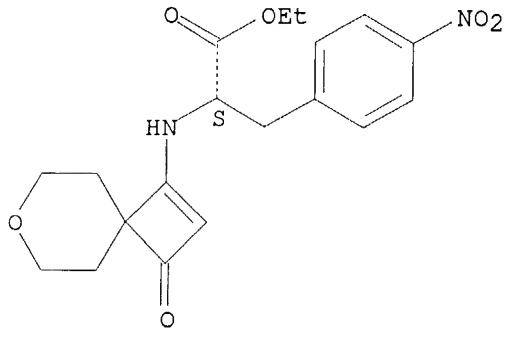
RN 644995-09-5 CAPLUS
CN L-Phenylalanine, 4-amino-N-(3-oxospiro[3.5]non-1-en-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



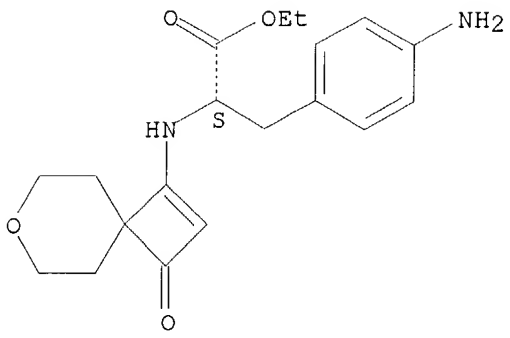
RN 644995-10-8 CAPLUS
CN L-Phenylalanine, 4-nitro-N-(3-oxo-7-oxaspiro[3.5]non-1-en-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



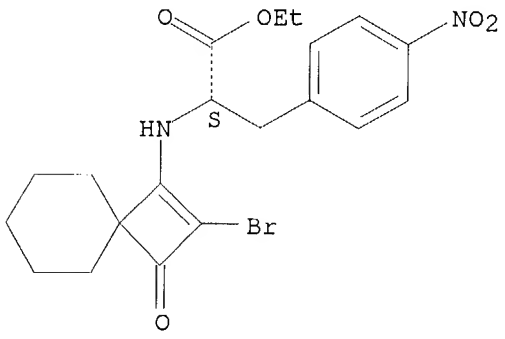
RN 644995-11-9 CAPLUS
CN L-Phenylalanine, 4-amino-N-(3-oxo-7-oxaspiro[3.5]non-1-en-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



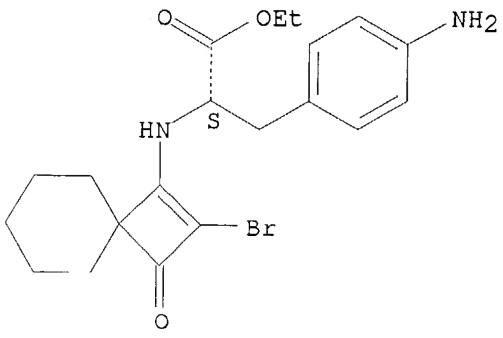
RN 644995-12-0 CAPLUS
CN L-Phenylalanine, N-(2-bromo-3-oxospiro[3.5]non-1-en-1-yl)-4-nitro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



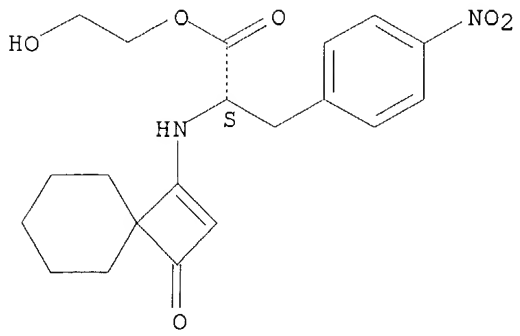
RN 644995-13-1 CAPLUS
CN L-Phenylalanine, 4-amino-N-(2-bromo-3-oxospiro[3.5]non-1-en-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



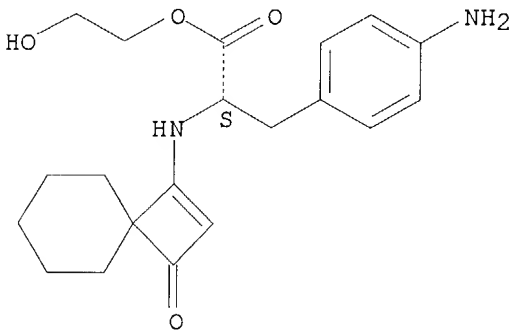
RN 644995-15-3 CAPLUS
CN L-Phenylalanine, 4-nitro-N-(3-oxospiro[3.5]non-1-en-1-yl)-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 644995-16-4 CAPLUS
CN L-Phenylalanine, 4-amino-N-(3-oxospiro[3.5]non-1-en-1-yl)-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d re 1-3

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
RE
(1) American Home Prod; WO 0035855 A 2000 CAPLUS
(2) Celltech R & D Ltd; WO 02068393 A 2002 CAPLUS
(3) Peter, A; WO 0073260 A 2000 CAPLUS

=>